REMARKS

The Office Action of October 15, 2009 has been carefully considered.

Claims 1-39 have been canceled and replaced by a new set of claims 40-58. New claim 40 replaces claim 1, and incorporates recitations from original claims 1, 2, and 3, in which substituent Q is limited in view of the examples. Claims 41-45 correspond to original claims 4 and 6-10, respectively, claims 46-51 correspond to original claims 12-17, respectively, claims 52-55 correspond to original claims 28-31, respectively, and claims 56-58 are directed to compounds which are exemplified in the present specification.

Since claims 15-17 and 28-31 were noted as being withdrawn from consideration in the Office Action, the corresponding new claims are so designated. However, Applicants believe that these claims should be examined as they are not inconsistent with the elected species.

Claims 1-14 have been rejected under 35 USC 112, 2nd paragraph, as indefinite as not reciting a specific point of attachment for susbstituents, in particular the "Z" group.

However, Applicants believe that, in keeping with convention, it is clear to one of ordinary skill in the art that radical "Z" may be attached to "Q" by any carbon atom of the phenyl ring which is not substituted by R_8 or $(R_9)_p$.

Withdrawal of this rejection is requested.

Claims 1-14 have been rejected under 35 USC 112, 1st paragraph, on the basis that there is no enablement provided for the entire scope of claimed compounds.

As note above, new claim 40 has been limited to those elected compounds for which enablement has been provided by the examples of the specification.

Withdrawal of this rejection is requested.

Claims 1-14 have been rejected under 35 USC 103(a) over Okada in view of Wermuth, Strehlke et al, Bowman et al '672 and Bowman et al '250.

The invention is directed to imidazole derivatives which are aromatase inhibitors; some of the compounds are also sulfatase inhibitors.

Okada has been cited to show aromatase inhibitors which are triazole derivatives with substituents which overlap the substituents of the imidazole derivatives of the invention.

The Office action states that the difference between examples 22 and 68 of Okada and the claimed compounds is the substitution of a triazole ring in Okada by an imidazole ring of the invention.

In both cases, the -N= of the triazole ring in Okada was replaced with a -CH= group in the invention.

Strehlke et al relates to N-substituted imidazoles having aromatase inhibiting properties. The compounds of formula (I) of Strehlke et al have no tertiary amine, whereas the compounds of the present invention do have a tertiary amine.

Bowman et al '672 relates to alpha-heterocyclic substituted tolunitriles and particularly to triazole derivatives of formula (V) as defined in claim 2 (column 34).

Bowman et al '250 also relates to alpha-heterocyclic substituted tolunitriles, and in particular to imidazole derivatives of formula (II) as defined in claim 3 (column 28).

As with the compounds of US patent Strehlke et al, the compounds of Bowman et al patents have no tertiary amine, contrary to the compounds of the claimed invention.

Wermuth relates to molecular variations based on isosteric replacements and states on page 211 that "the substitution of -CH= by -N= or -CH=CH- by -S- in aromatic rings has been one of the most successful applications of

classical isoterism."

However, after some examples, Wermuth points out on the same page that "[i]n all these cases no *essential* activity difference is found between the original drug and its isostere. However, it can happen that the procedure fails. Binder et al. for example, reported that thieno[2,3-*d*]isoxazole-3-methanesulfonamide, the thiophene analogue of the anticonvulsant drug zonisamide… was practically inactive against pentetrazole- electric shock-induced convulsions in mice, even at high doses."

Thus, one of ordinary skill in the art could reasonably expect equivalent activity, superior activity or no activity at all in performing the replacement of a triazole ring by an imidazole ring in a given molecule. There would be no way to determine the activity without testing.

The Office Action also makes reference to table 13.6 on page 212, which refers to ring equivalents. In particular, Wermuth specifies that imidazole ring would be a ring equivalent of 1,2,4-triazole (see second line of this table), based on the article of Alonso et al. (ref. 17), which actually shows that the imidazole bioisotere of ribavirin (triazole derivative) was less active or even inactive in comparison with ribavirin (see pages 836-837 the paragraph entitled "antiviral results and discussion" of Alonso et al, copy enclosed.

Thus, the allegation that imidazoles and triazoles are equivalents in pharmaceuticals is mere speculation. One of ordinary skill in the art could not assume equivalence, or even any activity for a given purpose, without actual testing.

In this regard, Applicants submit herewith a Declaration under 37 CFR 1.132 of inventor Jacqueline Shields. As reported in the declaration, a direct comparison was made between

Example 45 of the present application, and a corresponding triazole. The compound of the invention was found to be superior in both aromatase and sufatase activity. The sulfatase activity is not suggested by Okada et al.

The declaration also discusses the activity of the claimed compounds compared with anastrozole and letrozole, anastrozole being the most clinically used aromatase inhibitor for hormone-dependent breast cancer. This comparison is found in Table 1 of the application for certain compounds of the invention, and in the tables of the declaration for other compounds found in the examples, as well as compounds according to the invention not previously found in the examples. The compounds in general had aromatase activity, and some of the compounds had sulfatase activity as well.

In support of the allegation of obviousness, the Office Action cites the standards for proof of obviousness given in *Eisai Co. Ltd. v. Dr. Reddy's Laboratories Ltd.*, 87 USPQ2d 1454 (Fed. Cir. 2008). In fact, *Eisai* upheld the finding of the trial court that the compounds in question were not obvious despite the structural similarities.

Given the well known level of unpredictability in the pharmaceutical art, Applicants submit that it would not have been obvious that the claimed compounds would have aromatase and sulfatase inhibiting activity based on the cited art, and withdrawal of this rejection is requested.

Claims 1-14 have been rejected on grounds of non-statutory obviousness-type double patenting over claims 1-24 of US 6,737,433.

There is no overlap between the compounds of US 6,737,433 and the claims of the present application either as filed or after restriction.

Furthermore, contrary to the allegation, the differences

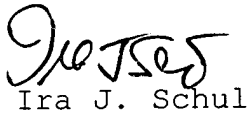
between the two lists of substituents are not obvious variations.

The present compounds are distinct from the compounds of US patent 6,737,433 and should not be considered at all as obvious variations, as the compounds of US patent 6,737,433 are only aromatase inhibitors, the claimed compounds include potent aromatase and sulfatase inhibitors. Some of the inventive compounds with a hydroxy group are metabolites of inventive compounds having both aromatase and sulfatase activities.

Withdrawal of this rejection is requested.

In view of the foregoing amendments and remarks, Applicants submit that the present application is now in condition for allowance. An early allowance of the application with amended claims is earnestly solicited.

Respectfully submitted,



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